

CMV primary episode analysis

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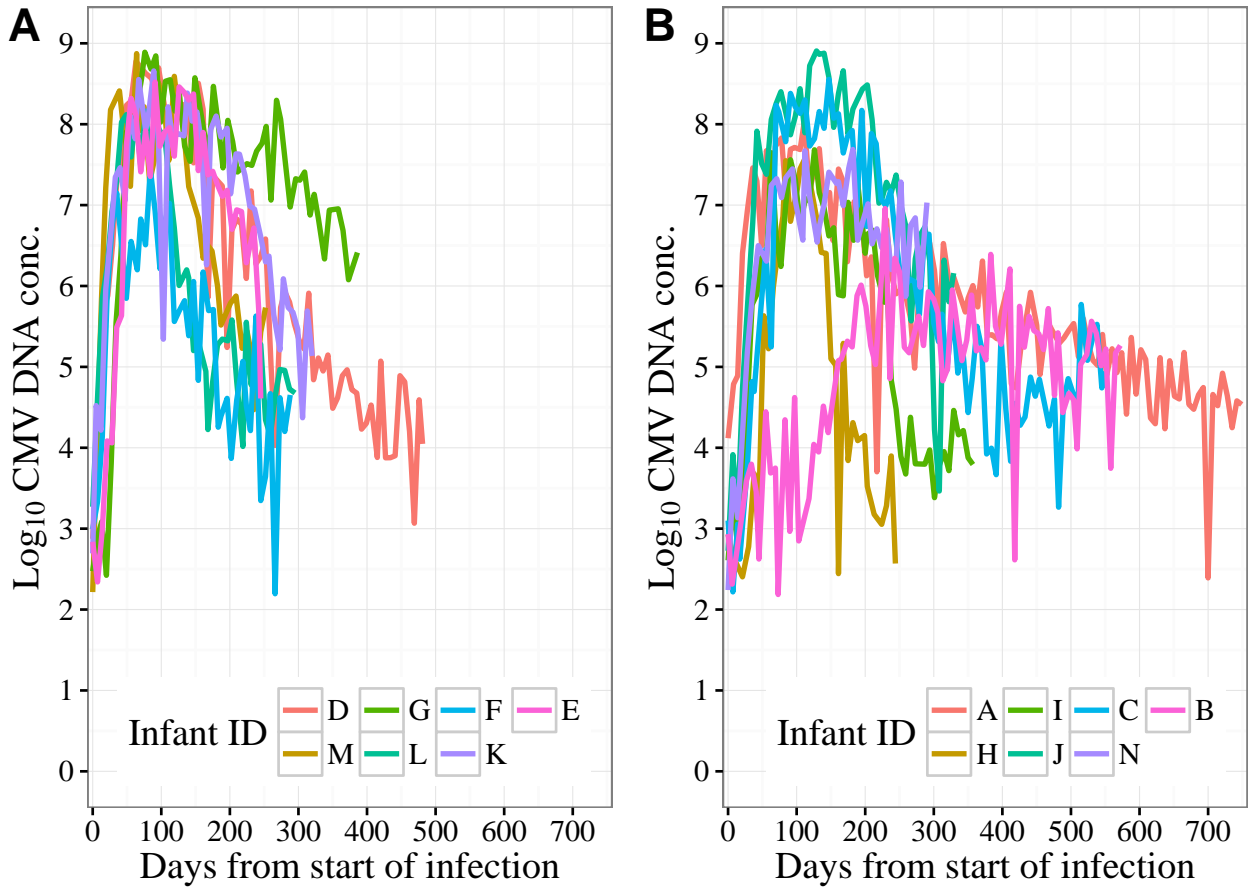
Contents

Description	1
Overview of the data	2
General statistics, peak shedding, duration	2
Comparison of oral and plasma shedding	4
Three phase classification	5
Raw results	6
Raw phase regression results	6
Summary of three phases	6
Compare three phase to two phase	7
Plot of features	8
Cubic model of clearance and rebound analysis	9
Correlation analysis	10
Age and features	10
Mother HIV	10
Saving figures and table	10
Figures	10

Description

This is the main analysis of the primary CMV oral shedding episodes. Here, we extract key characteristics of the shedding episodes (e.g., peak load), determine the cutoffs for the three phases, analyze correlation between features, and analyze rebound behavior.

Overview of the data



General statistics, peak shedding, duration

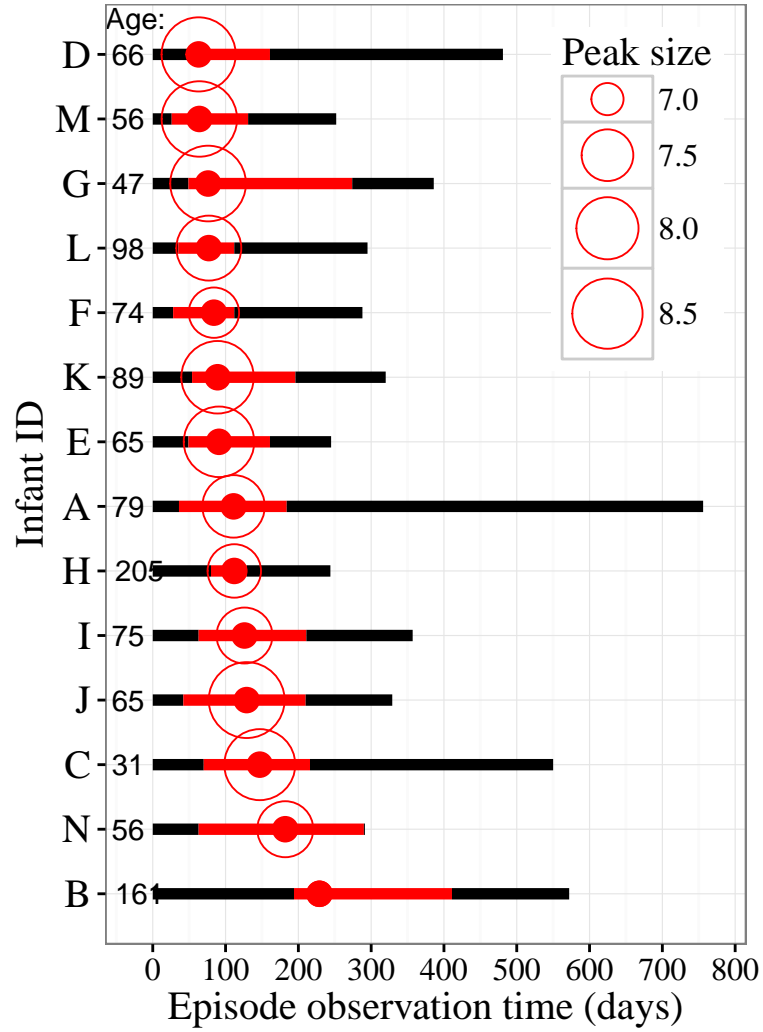
	n	14
total negative swabs		4
median age (range) days		70 (31, 205)
percent mothers hiv +		50
total oral swabs		763
total plasma swabs		52
median duration (range) days		324.5 (244, 756)
median peak shedding duration (range) weeks		20.57 (7, 32.43)
median first positive (range) log10 conc.		2.86 (2.22, 4.12)
median peak shedding (range) log10 conc.		8.34 (6.96, 8.91)

Table 1: Summary statistics

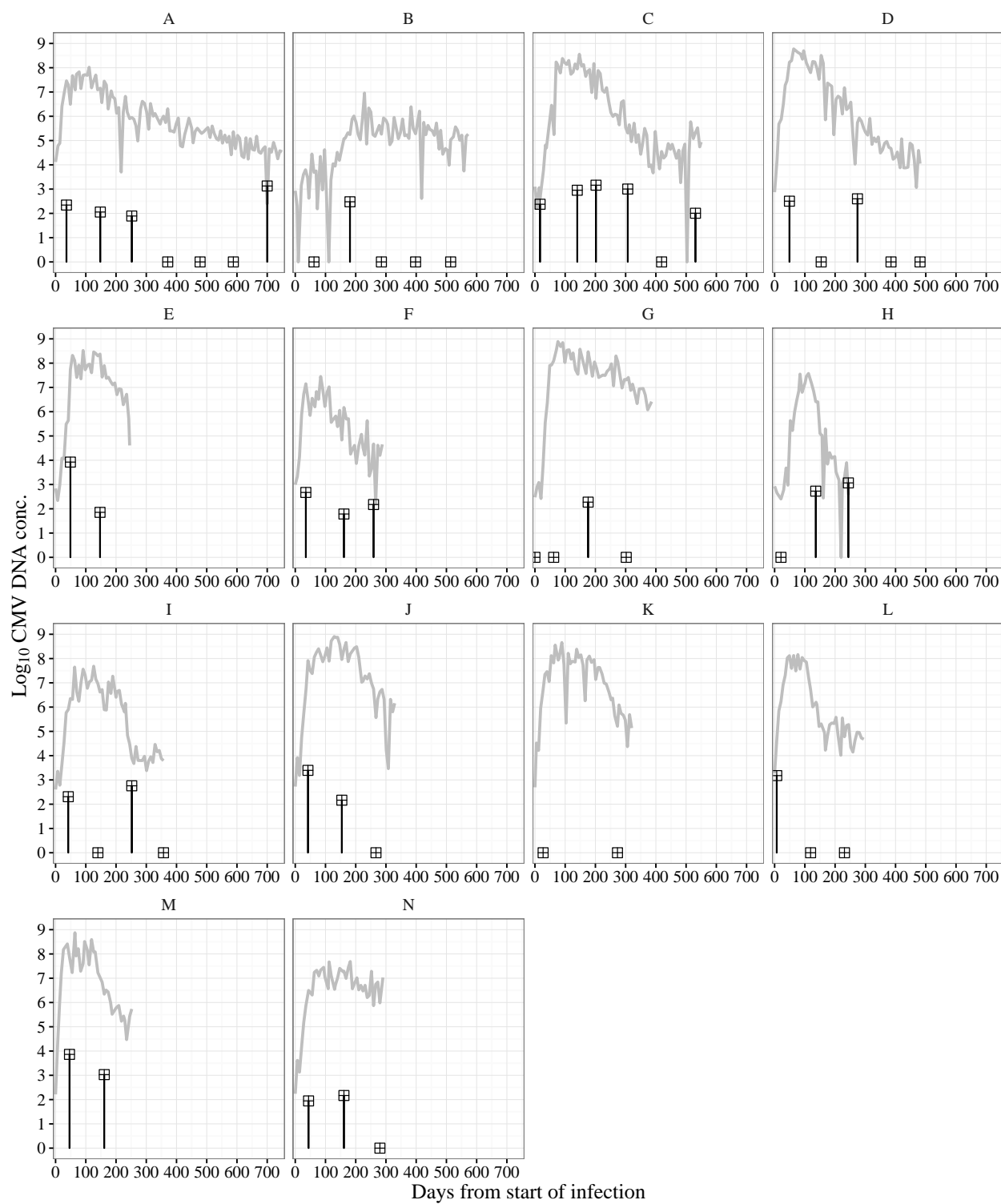
PatientID2	n	days
B	2	10, 111
C	1	503
H	1	220

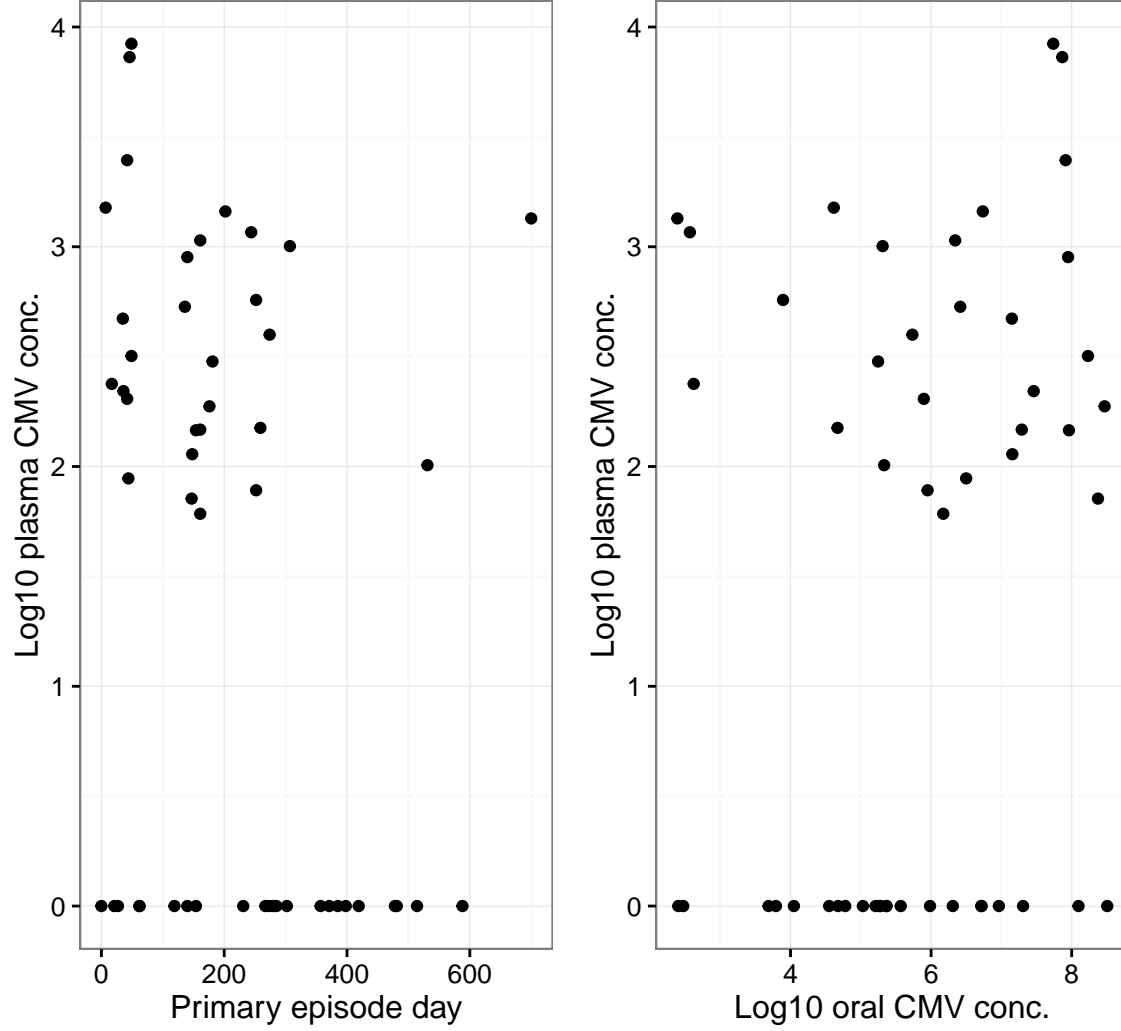
Table 2: Negative swabs

red region denotes shedding within 1 log



Comparison of oral and plasma shedding





total oral swabs	763
total plasma swabs	52
total positive plasma swabs	0
percent positive plasma swabs	55.76923
median log10 pls viral load (range)	2.5 (1.78, 3.92)
Pearson correlation with oral	0.22 (95% CI: -0.06, 0.46)
Spearman correlation with oral	0.19 (95% CI: -0.11, 0.48)
Pearson correlation with oral (pos plasma only)	-0.04 (95% CI: -0.4, 0.33)
Spearman correlation with oral (pos plasma only)	-0.12 (95% CI: -0.47, 0.28)
lmm oral count ~ binary pls predictor	0.81 (95% CI: -0.11, 1.73)

Table 3: Plasma load analysis

Three phase classification

Each episode has three characteristic phases:

1. expansion: oral episode start to 1 log before the peak

2. transition: 1 log before the peak until the peak
3. clearance: peak until end of observation

Raw results

Raw phase regression results

	PatientID2	expansion_n	expansion_slope_95pctCI	expansion_rsqr	double_time_days
1	A	6	0.7 (0.49, 0.9)	0.96	0.43
2	B	29	0.1 (0.07, 0.13)	0.63	3.11
3	C	11	0.5 (0.34, 0.67)	0.84	0.60
4	D	8	0.72 (0.55, 0.89)	0.95	0.42
5	E	8	0.69 (0.45, 0.94)	0.89	0.43
6	F	5	1 (0.58, 1.42)	0.95	0.30
7	G	8	0.78 (0.45, 1.1)	0.85	0.39
8	H	11	0.41 (0.26, 0.56)	0.81	0.73
9	I	10	0.56 (0.44, 0.67)	0.94	0.54
10	J	7	0.84 (0.57, 1.12)	0.93	0.36
11	K	9	0.63 (0.41, 0.85)	0.87	0.48
12	L	6	0.78 (0.51, 1.05)	0.94	0.38
13	M	5	1.62 (1.2, 2.04)	0.98	0.19
14	N	9	0.53 (0.39, 0.67)	0.92	0.57

Table 4: Raw results from expansion phase regression

	PatientID2	trans_n	trans_slope_95pctCI	trans_rsqr
1	A	12	0.07 (0, 0.13)	0.31
2	B	6	0.14 (-0.32, 0.6)	0.15
3	C	12	0 (-0.05, 0.05)	0.00
4	D	3	0.27 (-1.32, 1.86)	0.82
5	E	7	0.01 (-0.23, 0.24)	0.00
6	F	9	0.03 (-0.12, 0.18)	0.03
7	G	5	0.26 (0.12, 0.41)	0.92
8	H	6	0.1 (-0.12, 0.33)	0.29
9	I	10	0.04 (-0.08, 0.16)	0.07
10	J	13	0.08 (0.03, 0.13)	0.51
11	K	6	0.07 (-0.17, 0.31)	0.15
12	L	7	0.05 (-0.13, 0.23)	0.11
13	M	5	0.02 (-0.52, 0.56)	0.00
14	N	18	0.01 (-0.03, 0.04)	0.01

Table 5: Raw results from transition phase regression

Summary of three phases

Infant B had the lowest expansion R2 of 0.6276844 . Infant B had the a low clearance R2 of 0.1646749 . Infant N had the a low clearance R2 of 0.1028881 .

	PatientID2	clr_n	clr_slope_days_95pctCI	half_life_days	clr_rsqr
1	A	92	-0.03 (-0.03, -0.02)	10.41	0.68
2	B	48	-0.02 (-0.03, -0.01)	15.30	0.16
3	C	59	-0.06 (-0.08, -0.05)	4.69	0.67
4	D	58	-0.08 (-0.09, -0.08)	3.57	0.85
5	E	23	-0.12 (-0.15, -0.08)	2.59	0.72
6	F	30	-0.11 (-0.14, -0.08)	2.82	0.64
7	G	39	-0.05 (-0.06, -0.04)	6.42	0.74
8	H	20	-0.23 (-0.31, -0.16)	1.30	0.72
9	I	33	-0.12 (-0.15, -0.1)	2.46	0.78
10	J	30	-0.13 (-0.16, -0.1)	2.26	0.75
11	K	34	-0.09 (-0.12, -0.06)	3.38	0.59
12	L	32	-0.11 (-0.13, -0.08)	2.84	0.66
13	M	26	-0.14 (-0.16, -0.11)	2.20	0.84
14	N	16	-0.03 (-0.08, 0.02)	9.67	0.10

Table 6: Raw results from clearance phase regression

	Expansion	Transition	Clearance
Median duration (range) wk.	7 (3.71, 27.71)	6 (2, 17)	32.07 (15.43, 92.14)
Median swab change (range) wk.	0.64 (-1.77, 2.99)	0.09 (-1.03, 1.64)	-0.07 (-3.6, 3.13)
Median slope (range) wk.	0.7 (0.1, 1.62)	0.06 (0, 0.27)	-0.1 (-0.23, -0.02)
Median double/half-time (range) wk.	0.43 (0.19, 3.11)	NA (NA, NA)	3.11 (1.3, 15.3)
Median R-square (range)	0.92 (0.63, 0.98)	0.13 (0, 0.92)	0.7 (0.1, 0.85)

Table 7: Summary of phase features

Compare three phase to two phase

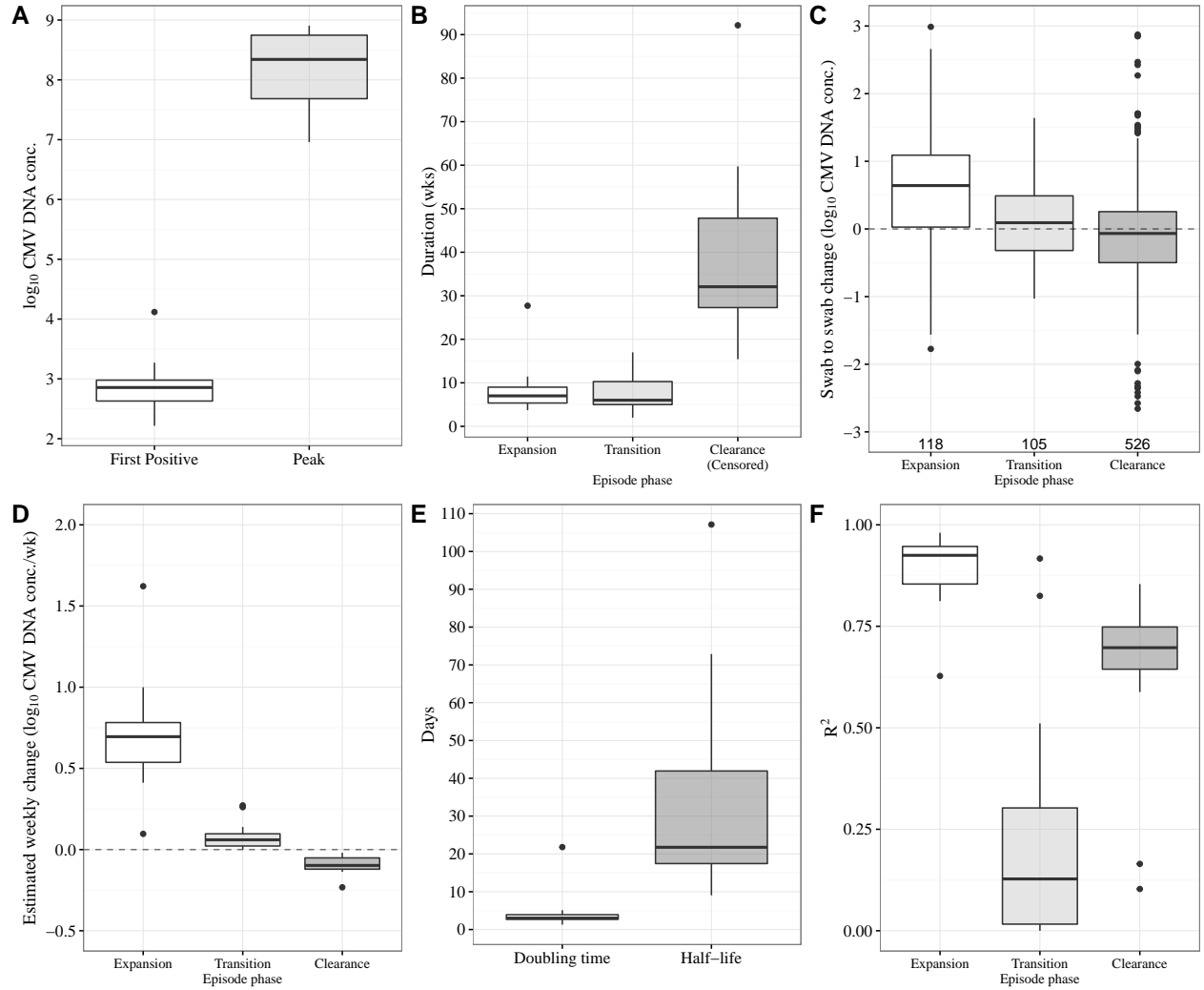
The three phase classification comes from an apparent transition phase between the start of the episode and the peak viral load. In the biphasic classification, expansion phase ends at peak (instead of 1 log before peak). The R-square values are generally worse when we make that assumption.

11 episodes perform better with transition phase

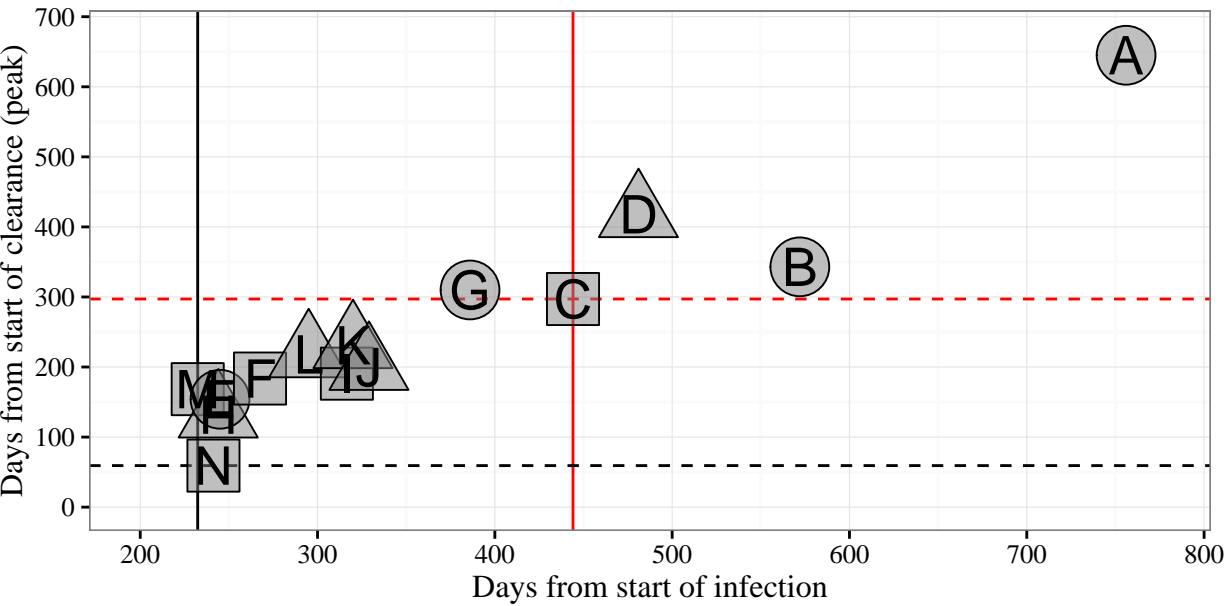
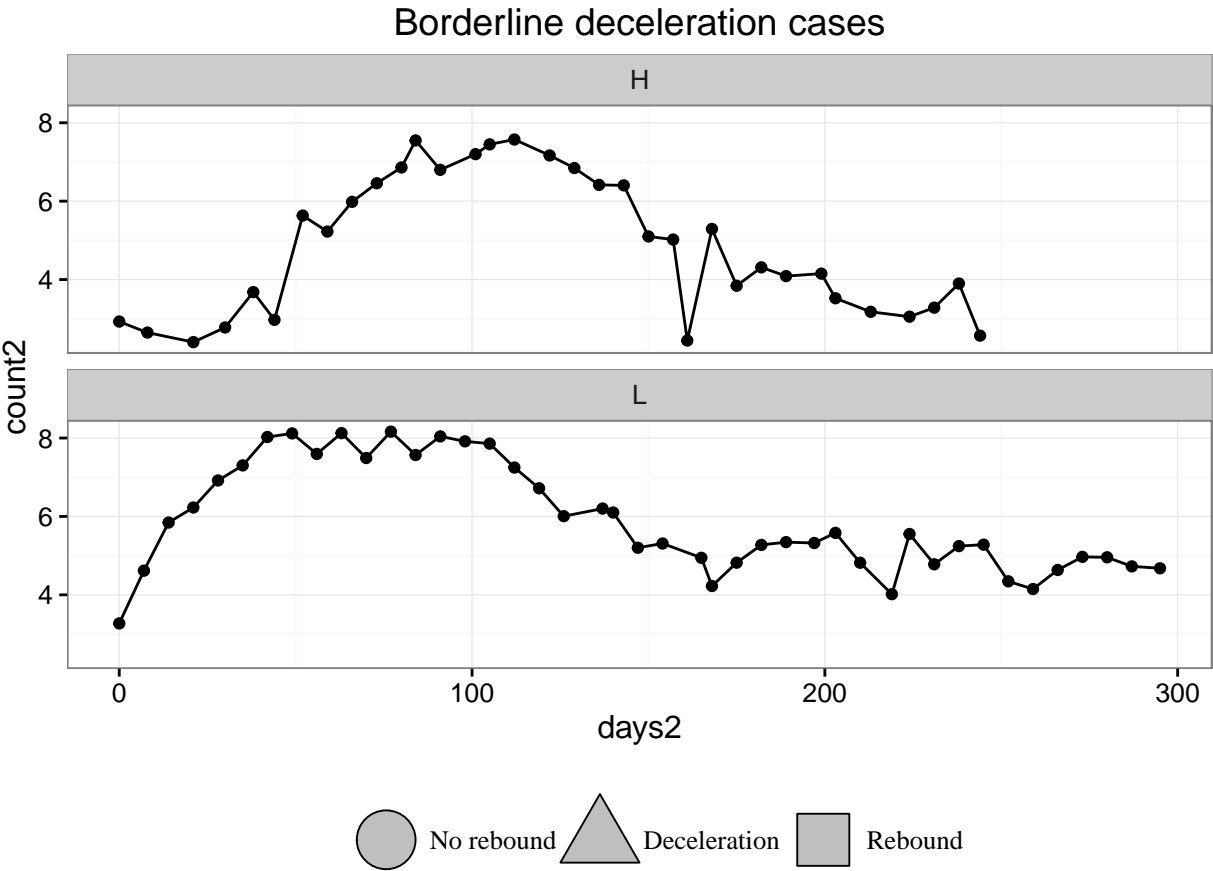
Infant ID	Growth to peak	Growth to 1 log before peak	Triphasic > biphasic
A	0.67	0.96	TRUE
B	0.72	0.63	FALSE
C	0.80	0.84	TRUE
D	0.94	0.95	TRUE
E	0.85	0.89	TRUE
F	0.61	0.95	TRUE
G	0.93	0.85	FALSE
H	0.88	0.81	FALSE
I	0.76	0.94	TRUE
J	0.74	0.93	TRUE
K	0.79	0.87	TRUE
L	0.75	0.94	TRUE
M	0.65	0.98	TRUE
N	0.59	0.92	TRUE

Table 8: R-square comparing growth in two phase vs three phase classification

Plot of features



Cubic model of clearance and rebound analysis



Pair1	Pair2	raw_cor	p_value	boot_cor	boot_lower
Infection age (days)	Peak (log10 CMV DNA copies/mL)	-0.396	0.202	-0.381	-
Infection age (days)	Expansion duration (days)	-0.285	0.369	-0.292	-
Infection age (days)	Transition duration (days)	-0.156	0.627	-0.161	-
Infection age (days)	Clearance duration (days)	0.190	0.555	0.193	-
Peak (log10 CMV DNA copies/mL)	Expansion duration (days)	-0.095	0.768	-0.103	-
Peak (log10 CMV DNA copies/mL)	Transition duration (days)	-0.382	0.221	-0.382	-
Peak (log10 CMV DNA copies/mL)	Clearance duration (days)	0.084	0.795	0.086	-
Expansion duration (days)	Transition duration (days)	0.247	0.438	0.272	-
Expansion duration (days)	Clearance duration (days)	0.161	0.618	0.151	-
Transition duration (days)	Clearance duration (days)	-0.284	0.371	-0.303	-

Table 9: Spearman Correlations - excluded 2 older infants. Bootstrap takes median.

Pair1	Pair2	raw_cor	p_value	boot_cor	boot_lower
Infection age (days)	Peak (log10 CMV DNA copies/mL)	-0.590	0.026	-0.586	-
Infection age (days)	Expansion duration (days)	0.192	0.512	0.202	-
Infection age (days)	Transition duration (days)	-0.308	0.284	-0.302	-
Infection age (days)	Clearance duration (days)	0.044	0.881	0.049	-
Peak (log10 CMV DNA copies/mL)	Expansion duration (days)	-0.385	0.175	-0.393	-
Peak (log10 CMV DNA copies/mL)	Transition duration (days)	-0.104	0.725	-0.103	-
Peak (log10 CMV DNA copies/mL)	Clearance duration (days)	0.095	0.748	0.093	-
Expansion duration (days)	Transition duration (days)	-0.089	0.763	-0.091	-
Expansion duration (days)	Clearance duration (days)	0.056	0.848	0.050	-
Transition duration (days)	Clearance duration (days)	-0.202	0.489	-0.217	-

Table 10: Spearman Correlations - all data. Bootstrap takes median.

Correlation analysis

Age and features

Mother HIV

Outcome	Estimate	P-value
Infection age (days)	-1.29 (-57.32, 54.75)	0.961
Peak (log10 CMV DNA copies/mL)	0.19 (-0.57, 0.96)	0.588
Expansion duration (days)	-6.86 (-57.19, 43.48)	0.772
Transition duration (days)	3.71 (-30.55, 37.98)	0.817
Clearance duration (days)	-97 (-259.87, 65.87)	0.219

Table 11: Linear model (unadjusted) with momhiv (reference = neg) as predictor.

Saving figures and table

See code, won't save new tables or figures unless the save_output_figs and save_output_tables variables are changed to TRUE.

Figures